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dual's genetic value at the QTL is used in the linkage analysis instead of his phenotypic observations.

John D. Boughter Jr.,[33] Glayde Whitney,[33] and David B. Harder.[33] C3.SW-*Soa*^{a} Congenic Taster Mice: Manifestations of the Bitter Taste Gene.[34] Sensitivity to the bitter acetylated sugar sucrose octaacetate (SOA) is mediated by a single locus system with three alleles in mice. Inbred strains are classified according to SOA phenotype as tasters, nontasters, or demitasters (intermediate sensitivity). We have created a congenic strain, C3.SW-*Soa*^{a}, from taster (SWR/J) and demitaster (C3HeB/FeJ) strains (J. D. Boughter Jr. and Glayde Whitney, 1994, *Chem. Senses,* 19, 444–445). The C3 inbreds provide a suitable background for investigating genetic influences on bitter taste because they are relatively insensitive to many bitter compounds. The resulting congenic mice carry the tasting allele on a 99% C3 demitaster background. In several experiments we tested C3.SW, C3, and SW mice with concentration series of SOA and various bitter substances (48-h preference tests). Variation at the *Soa* locus strongly influenced sensitivity to SOA, and other bitter substances including strychnine, brucine, quinine, and denatonium benzoate. These results are consistent with the hypothesis that the *Soa* gene mechanism influences responsiveness to a broad class of generally bitter tastants.

K. Brandon[35] and R. J. Rose.[36] A Multivariate Twin Family Study of the Genetic and Environmental Structure of Personality, Beliefs, and Alcohol Use.[37] Sources of variation in behaviors, personality and attitudes related to alcohol use and its abuse were studied within a twin-family design to examine the covariance of behavioral disinhibition, religiosity, and antisocial personality. A sample of 523 monozygotic and dizygotic young adult twin pairs, 198 nontwin same-gender sibling pairs, and subsets of the twins' and siblings' parents completed questionnaires regarding use of alcohol, frequency and type of interpersonal contact, and MMPI scales of antisocial personality (Pd), behavioral disinhibition (MAC), and religious belief (REL). Model-fitting techniques tested hypotheses about sources of trait variation and mechanisms of transmission of personality traits and religiosity from parent to offspring. Common genetic and environmental pathways for covariation between traits were evaluated. Significant genetic contributions to individual differences in religiosity, behavioral disinhibition, and antisocial personality were found, with variability in religiosity partially explained by common environments of siblings. Cultural transmission from parent to offspring was significant only for behavioral disinhibition. Covariation between behavioral disinhibition and antisocial personality and that between behavioral disinhibition and religiosity was partly explained by common genetic effects.

K. K. Bucholz,[38] A. C. Heath,[38] T. Reich,[38] V. M. Hesselbrock,[39] J. Kramer,[40] and J. I. Nurnberger Jr.[41] Subtyping Alcoholism Using Latent Class Analysis with Data from a Multicenter Family Study of Alcoholism.[42] The heterogeneity of alcoholism challenges treatment efficacy researchers and geneticists to identify homogenous subtypes for analysis. We explored the existence of distinctive subtypes of alcoholics using latent class analysis with data from 2551 relatives of alcoholic probands, all participants in the Collaborative Study of the Genetics of Alcoholism (COGA). Data on 37 symptoms of alcohol dependence from 1360 female and 1191 male relatives were analyzed, with a four-class solution selected as the best fitting among the two- through six-class solutions that were examined. The more complex solutions yielded small classes with few individuals. The four latent classes and the prevalence of each were as follows: Class 1, nonproblem drinkers (37.8% M, 50% F); Class 2, heavy drinkers (persistent desire to stop, having tolerance and blackouts) (31.1% M, 28.8% F); Class 3, heavy drinkers with social problems and some health and emotional problems (19.9% M, 14.6% F); and Class 4, severely affected alcoholics, with physiological dependence, inability to stop drinking, craving, and health and emotional problems (11.2% M, 6.7% F). A majority of Class 2 (and nearly all in Classes 3 and 4) qualified for DSM-3R alcohol dependence, suggesting a bimodal distribution of drinkers and alcoholics, with little nonalcoholic problem drinking. We conclude that alcoholism is not differentiated by distinctive symptom profiles but rather lies on a continuum of severity, with the possible exception of withdrawal. Analyses will be conducted to determine whether our conclusion holds when family resemblance is taken into account.

Abel Bult[43] and Eddy A. Van der Zee.[44] Proposing a Model for the Neural Regulation of Nest-Building Behavior, Circadian Rhythmicity, and Aggression in Selected House Mouse Lines. Artificially selected lines can be a useful tool in studying the neural basis of behavior. Differences, in the behavior under selection, between low- and high-selected lines may become large enough to detect underlying changes in brain function which might be undetectable in a natural population otherwise. Replicated bidirectional selection for thermoregulatory nest-building behavior in the house mouse, for more than 55 generations, resulted in a 40-fold difference between the high- and the low-selected lines. These mice differ, besides nest-building behavior, in circadian rhythm parameters of wheel running (Bult *et al.*, 1993, *Brain Res. Bull.*, 32, 623–627) and level of aggression (Sluyter et al., *Behav. Genet.*, 1995, in press). Of the various neurochemical substances studied in the brain, arginin-vasopressin (AVP), protein kinase C (PKC), and STEP, a protein tyrosine phosphatase, have been shown to differ between the lines. AVP plays a role in circadian rhythmicity, aggression, and thermoregulation, and PKC is expressed in AVP and AVP-recipient cells (Van der Zee and Bult, in prep.). The physio-

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logical role of STEP is currently under investigation. The numbers of AVP-immunoreactive (AVP-ir) and AVP-recipient neurons differ in the suprachiasmatic nuclei (SCN). The low-selected mice have a 1.5-fold higher number of AVP-ir neurons compared to the high-selected and control mice (Bult *et al.*, 1992, *Brain Res.*, 578, 335–338). The level of PKCα and PKCβ1 in the SCN is also higher in the low-selected compared to the high-selected lines but control lines are intermediate, whereas no differences were found for PKCβ2 and PKCγ (Bult *et al.*, 1991, *Behav. Genet.*, 21, 563; unpublished data). Preliminary data indicate that high-selected and control lines have a 40–50% higher level of STEP-ir in the lateral septum compared to the low-selected lines. Using the neuroanatomical correlates with behavior and the general knowledge of brain function as a basis, we will present a model in which we propose a mechanism by which nest-building behavior, circadian rhythmicity, and aggression are regulated.

K. A. Buss,[45] J. Bihun,[45] K. S. Lemery,[45] and H. H. Goldsmith.[45] Genetic and Environmental Contributions to Emotional Reactivity in Infants, Toddlers, and Preschoolers.[46] Data from over 660 pairs of infant, toddler, and preschooler twins were analyzed to study the genetic and environmental contributions to emotional reactivity. Emotional reactivity was assessed through factor analysis of three age-appropriate temperament questionnaires: Rothbart's *Infant Behavior Questionnaire*, Goldsmith's *Toddler Behavior Assessment Questionnaire*, and Rothbart's *Children's Behavior Questionnaire*. Factor analysis of the 6-scale IBQ revealed two factors: Negative Emotional Reactivity and Positive Emotional Reactivity. Factor analysis of the five-scale TBAQ revealed two factors: Negative Emotional Reactivity and Positive Emotional Reactivity. Factor analysis of the 16-scale CBQ revealed three factors: Surgency, Negative Affectivity, and Effortful Control (a type of emotional regulation). Using "calibration" samples of singletons, correlations of conceptually similar factors across the three questionnaires were moderate (ranging from .35 to .65). Using DF regression analyses, the factors encompassing negative emotional reactivity have moderate genetic underpinnings for the IBQ, TBAQ, and CBQ. In addition to moderate effects of heritability, we found evidence for moderate effects of shared environment for early positive emotional reactivity as measured by the IBQ and TBAQ. In an attempt to elucidate the sources of this shared environment influence, we examined the positive and negative affect dimensions of Halberstadt's (1986) *Family Expressiveness Questionnaire* (FEQ).

Gregory Carey.[47] Analytical Methods for the Application of Molecular Genetic Strategies to Quantitative Phenotypes.[48] Molecular genetics has made great strides in the medical sciences. The process of discovery generally has begun with the identification of informative pedigrees where the disorder is known or suspected to run in a Mendelian fashion. A positive linkage is then followed up by often painstaking and time-consuming isolation of the relevant locus. An alternate strategy, the association study, generally uses a polymorphism at a candidate locus to test for different allele frequencies among those with and without the disorder. Here, I present a analytical strategy that combines the association with the linkage design for quantitative traits in general pedigrees. Several association loci and several linkage loci may be simultaneously analyzed along with several phenotypic measures of the trait of interest. The technique permits evaluation of several loci in a single statistical test and increases the power for detecting molecular genetic effects more than individual tests for each locus. Rather than relying on exact likelihood functions, the method uses approximations based on the assumption of a computationally tractable and efficient multivariate distribution conditional on genotype (e.g., multivariate normal or multivariate *t*). There is little bias in the approximation over a wide area of the parameter space. The area of significant bias is associated with a rare recessive gene of very large effect that generates two different quantitative distribution. The advantage of the technique is that it permits evaluation of strong hypotheses about behavior. For example, it would be possible to simultaneously test whether the multiple loci that contribute to the dopamine system contribute to a relevant behavior.

Gregory Carey,[49] Michael C. Stallings,[49] John K. Hewitt,[49] and David W. Fulker.[49] The Familial Relationship Among Personality, Substance Abuse, and Other Problem Behavior in Adolescents.[50] Theorists such as Eysenck, Gray, Cloninger, and Tellegen posit important relationships between higher-order personality traits and form of psychopathology and generally attribute a causal role to personality. Because personality and problem behavior run in families, it is a natural question to ask how much of the family transmission for problem behavior can be accounted for by the transmission of personality. We explore this issue by examining both Cloninger's higher-order traits and Tellegen's higher-order traits in a series of families with a substance abusing proband and a series of control families. Although both personality and problem behavior run in these families, personality explains only a small amount of the familial variances and covariances for drug and alcohol abuse, antisocial behavior, depression, and somatic complaints. This general pattern occurs under various estimates of measurement error for both personality and problem behavior. An intriguing side issue is the relationship between problem behavior and lower- versus higher-order personality traits. In these data, lower-order traits (e.g., aggression, impulsivity) predict problem behavior better than higher-order traits (e.g., extraversion, reward dependence).

K. A. Case,[51] T. Tritto,[51] and B. C. Dudek.[51] Common Genetic Influences on Psychomotor Stimulant Effects of Ethanol and Sodium Pentobarbital.[52] Sedative hypnotic drugs possess a paradoxical capability to produce behavioral arousal at a range of doses below those with noticeable sedative properties. This capability has been argued to be a key feature of some genetically distinct etiologies of alcoholism. Genetic influences on psychomotor stimulant effects of alcohol and sodium pentobarbital have been reported, and there is reason to hypothesize a genetic correlation between these two drug effects in mice. In a pattern similar to their response to ethanol (EtOH), DBA/2Abg (D2) mice are known to respond to low doses of sodium

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